

**REMARKS****Status of the Claims**

Claims 1-2, 5, 7-8, and 23-24 are amended and claims 33-43 are new and should be part of the elected group. Each new claim is supported in the specification as-filed. Claims 6, 10-12, and 25-32 are withdrawn. Upon entry of this Amendment, claims 1-43 are pending, and elected claims 1-5, 7-9, 13-24, and 33-43 should be examined. No new matter has been added.

**Disclosure Objection**

The PTO objected to the Amendment of 27 August 2003, because it allegedly “introduces new matter into the disclosure.” See Final Office Action of November 18, 2003, page 3. Specifically, the PTO believes the as-filed specification does not support the language “1 to 30 amino acids substituted, deleted...;” “1 to 15 amino acids substituted, deleted...;” “1 to 5 amino acids substituted, deleted...;” and “washing condition of 1.0x SSCP, 0.1% SDS at 65°C.” Office Action, page 3. Applicants respectfully traverse this objection.

The as-filed specification provides support for each of the objected phrases. The language “1 to 30 amino acids substituted, deleted...” finds support in the as-filed specification, for example, on page 7, lines 11 and 14-25. Similarly, the recitation “1 to 15 amino acids substituted, deleted...” is supported, for example, on page 7, lines 12 and 14-25. The phrase “1 to 5 amino acids substituted, deleted...” finds support, for example, on page 7, lines 12-25. The language “washing condition of 1.0x SSCP, 0.1% SDS at 65°C” is supported, *inter alia*, at page 29, lines 22-23.

As each of the objected phrases finds support in the as-filed specification, the rejection is improper and should be withdrawn.

**Rejections- 35 U.S.C. § 112, first paragraph (Written Description, New Matter)**

Claims 1c, 2-7, 9, 13-24 were rejected under 35 U.S.C. §112, first paragraph, for alleged lack of written description. Office Action, page 3. Specifically, the PTO alleged that the as-filed specification does not support “1 to 30 amino acids substituted, deleted...(claim 1c);” “1 to 15 amino acids substituted, deleted...(claims 13,18);” “1 to 5 amino acids substituted, deleted...(claims 14,19);” and “washing condition of 1.0x SSCP, 0.1% SDS at 65°C (claims 17, 22). Office Action, page 4. Applicants respectfully traverse this rejection.

As outlined above, the as-filed specification provides support for each of the objected phrases. The language “1 to 30 amino acids substituted, deleted...” finds support in the as-filed specification, for example, on page 7, lines 11 and 14-25. Similarly, the recitation “1 to 15 amino acids substituted, deleted...” is supported, for example, on page 7, lines 12 and 14-25. The phrase “1 to 5 amino acids substituted, deleted...” finds support, for example, on page 7, lines 12-25. The language “washing condition of 1.0x SSCP, 0.1% SDS at 65°C” is supported, *inter alia*, at page 29, lines 22-23.

As each of the objected phrases finds support in the as-filed specification, the rejection is improper and should be withdrawn.

**Rejections- 35 U.S.C. § 102(b)**

Claim 8 remains rejected under 35 U.S.C. §102 (b) as allegedly anticipated by Noguchi et al. Office Action, page 4. In short, the PTO takes the position that “in the absence of clear hybridization conditions, any polynucleotide sequence will hybridize to SEQ ID NO: 1.” Office Action, page 5. As the present version of claim 8 avoids this issue, the rejection should be withdrawn.

**Rejections- 35 U.S.C. § 101 (Non-statutory subject matter)**

Claims 7-8 and 23-24 are rejected under 35 U.S.C. §101 as allegedly embracing non-statutory subject matter. Office Action, page 5. Specifically, the PTO maintains that the claims “are not limited to isolated and purified polypeptides and/or polynucleotides and

encompass the full length naturally occurring product and therefore reads on products of nature.” Office Action, page 5.

As the present version of the claims avoids this issue, the rejection should be withdrawn.

**Rejections- 35 U.S.C. § 101 (Utility)**

Claims 1-5, 7-9, and 13-24 remain rejected under 35 U.S.C. § 101 for alleged lack of a specific and substantial asserted utility or a well-established utility. Office Action, pages 5-7. Applicants respectfully traverse this rejection.

According to the PTO, the claimed invention lacks a specific, substantial, and credible utility, or alternatively, a well-established utility. Office Action, pages 5-7. For this type of rejection, because utilities are asserted in the application, the rejection must be supported by explanation and supporting evidence. MPEP § 2107. Otherwise a rejection is improper and should be withdrawn.

Such is the case here. For example, the specification teaches that the amino acid sequence encoding Delta1 is a novel type I cytokine receptor. Specification, page 5, lines 15-17. The specification discloses that the gene encoding Delta1 was cloned from lymphocyte, and furthermore, northern analysis revealed that it was expressed in the heart, lung, liver, and spleen, as well as in myeloid and lymphoid cell lines such as Ba/F3, DA-1 and CTLL2. The specification further discloses that the membrane proximal region of human EPOR can be replaced with that region from the inventive protein and the engineered protein can activate JAK2. See specification, page 5, lines 15-25. Therefore, the receptor-like protein of the present invention is described as playing a regulatory role in immunity and haematopoiesis, which, of course, is specific.

A. Yet, despite the specification’s asserted utilities, the PTO takes the position “The fact that the proximal region of human EPO receptor can be replaced with that region from the Delta1 and that the engineered protein can activate Janus kinase (JAK) 2 in response to EPO is questionable because the chimera comprising the extracellular region of

hEPOR/cytoplasmic region of Delta1 was inactive.” Office Action, page 6. Applicants traverse the basis of this rejection.

In order to make a utility rejection, the PTO must do more than merely question operability-it must set forth factual reasons which would lead one of ordinary skill in the art to question the objective truth of the statement of operability. MPEP § 2107.02.

Here, the PTO has not set forth any factual reason. Moreover, Applicants are not required to provide a mechanism for Janus kinase (JAK) 2 activity. For these reasons alone, the rejections are improper. However, the as-filed specification discloses that the chimera EDER was responsive to EPO in Examples 4-5. As the results of these examples reveal that the proximal region of Delta1 functions as a type I cytokine receptor superfamily, Delta 1 has a specific and asserted utility.

B. The PTO alleges “the specification never discloses a true ligand of Delta 1. Thus it would be unclear how to activate and/or inhibit this protein and therefore how to use it.” Office Action, page 6. Applicants traverse the grounds for this rejection.

The presence or absence of the disclosure of a specific ligand of Delta 1 is irrelevant for determining whether the claimed invention is supported by a specific, substantial, and credible utility, or alternatively, a well-established utility. Again, for this reason alone, the rejection is improper and should be withdrawn.

C. The PTO alleges “a tissue-specific marker or genetic marker is not specific and substantial utilities for Delta 1.” Office Action, page 6. Applicants respectfully traverse the grounds for this rejection.

According to the PTO’s Revised Interim Utility Guidelines Training Materials, methods for identifying compounds which bind to a specific receptor are not applicable to the general class of receptors, and therefore, such an asserted utility must be considered specific for this reason alone. See Utility Guidelines, Example 12, page 65, lines 1-6.

Applying the PTO's own utility standards, the present invention is described as making possible other specific utilities, namely, tools for purifying and/or cloning factors related to the functions of the immune system. For example, the specification discloses that the transcript encoding Delta 1 has been identified in the heart, brain, spleen, lung, kidney and testis, but not in skeletal muscle. See specification, Figure 4, and page 25, lines 15-18. Thus, Delta 1 is described as a tissue-specific marker, a specific utility. Additionally, the precise chromosomal location of Delta 1 has been determined. See specification, Example 7. Thus, the guidance from the present specification makes it possible to use Delta 1 as a genetic marker for many purposes, including gene mapping, cloning, and chromosomal aberration tests, each of which, of course, are specific utilities.

D. The PTO takes the position that "Applicants fail to submit a sequence comparison between Delta1 and the receptor protein of Pandey et al. and Park et al. For that reason it is not clear if Delta1 and the receptor protein of Pandey and Parks are the same." Office Action, page 7. Moreover, the PTO asserts "The specification as originally filed does not have support for TSLP ligand or IL-7 $\alpha$  receptor. Therefore, the specification as originally filed lacks a specific and substantial asserted utility or a well established utility." Office Action, page 7. Applicants respectfully traverse the basis for this rejection.

Applicants are not required to provide a sequence comparison between Delta1 and the receptor protein of Pandey et al. and Park et al. As the claims of the present invention neither recite "TSLP ligand" nor "IL-7 $\alpha$  receptor," it is irrelevant whether the as-filed specification does or does not provide support for "TSLP ligand" or "IL-7 $\alpha$  receptor." Moreover, whether or not the as-filed application supports "TSLP ligand" or "IL-7 $\alpha$  receptor" has no bearing on whether the claimed invention is supported by an asserted utility that is both specific and substantial. For these reasons, the rejection is improper.

Furthermore, the application asserts for the claimed invention a variety of utilities, each of which is specific and substantial, i.e., defines a real world use, for reasons that should need no explanation. Cf. MPEP 2107.01 I. Nevertheless, the instant application discloses a wealth of information addressing the receptor's biological function and physiological role.

For example, at page 5, lines 15-17, the application identifies the protein to be “a novel protein belonging to the type I cytokine receptor superfamily.” At page 3, lines 16-21, the application suggests that the protein “functions especially in the immune system as a signal transduction molecule, mediating signals from outside to the inside of the cell.” The application discloses in Figure 1 the putative signal sequence and the transmembrane domain of the protein. The Figure also specifies the locations of the box 1 and box 2 regions, which as explained in the specification at page 6, lines 10-13, are considered in the art “to be important in intracellular signal transduction, and in particular, box1 is considered to be important for interaction of Jak (Janus kinase) with cytokine receptors.” Moreover, the application suggests at page 5, lines 21-23, that the protein of the present invention “is involved in the signal transduction through JAK2 activation by forming a complex with heterologous receptors.” Indeed, the specification at page 5, lines 26-29 and 31-32 states that “the receptor-like protein is presumed to play a regulatory role in immunity and haematopoiesis,” and that the protein may be useful, for example, in “screening for compounds as drug candidates for immune system related diseases.” In particular, before the priority date of this application, it was known that JAK2 relates to leukemia and that JAK2 inhibitors are useful to treat such diseases, as shown in the attached references (Meydan et al. *Nature* 379: 645-648 (1996); Lacronique et al. *Science* 278: 1309-1312 (1997); Luo et al. *The EMBO Journal* 14(7): 1412-1420 (1995)). Therefore, it is highly useful to screen for antagonists of Delta1 that activates JAK2.

Thus, in view of the disclosure, a skilled artisan would recognize multiple “real world” contexts of use for compounds identified by screening assays employing the protein of the instant invention. Such “real world” contexts of use include, for example, modulating immune responses in lymphocyte cells expressing the protein. Therefore, a specific and substantial utility for the protein of the instant invention is found in screening assays employing the protein of the instant invention. As such, the claimed invention is supported by an asserted utility that is both specific and substantial and the instant rejection should be withdrawn.

As discussed above, the subject matter embraced by the elected claims are described as having specific, substantial, and credible utility. Neither evidence nor explanation shows otherwise. Therefore, the rejection is improper and should be withdrawn.

**Rejections- 35 U.S.C. § 112, first paragraph (enablement)**

Claims 1-5, 7-9, and 13-24 remain rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Office Action, pages 8-9. The PTO alleges “since the claimed invention is not supported by specific or substantial asserted utility, the specification does not enable any person skilled in the art to use the invention.” Office Action, page 8. Specifically, the PTO maintains “the specification would not support claims to polynucleotides encoding Delta1 polypeptides modified to an unlimited extent relative to those exemplified.” Office Action, page 8.

The present version of the claims avoid this issue. Therefore, the rejection should be withdrawn.

**Rejections- 35 U.S.C. § 112, first paragraph (written description)**

Claims 1, 5, 7-8, and 13-24 are rejected under 35 USC § 112, first paragraph, for alleged lack of written description. Office Action, pages 9-11.

The present version of the claims are believed to avoid the concerns addressed in the Office Action. As the present version of the claims meet the requirements for written description under 35 U.S.C. § 112, Applicants respectfully request reconsideration and withdrawal of the rejection.

**Claim Objections**

Claim 8 is objected to because “a nucleotide is a base, a sugar, and a phosphate. Nucleotides themselves cannot, by definition, at least 15 bases, they have one base.” Office Action, page 11. As the present version of the claim avoids this issue, the objection should be withdrawn.

**CONCLUSION**

Applicants respectfully request that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing the claims in condition for allowance. Applicants submit that the proposed claim amendments neither raise new issues nor necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Finally, Applicants submit that the entry of the amendment would place the application in better form for appeal.

If there are any questions concerning this application, the Examiner is courteously invited to contact the undersigned counsel.

Respectfully submitted,

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Attachment: Revised Interim Utility Guidelines, Example 12, pages 63-69



### **Example 12: Receptors**

**Specification:** The specification discloses a protein, isolated from a cell membrane preparation, which is the binding partner for protein X. The specification does not characterize the isolated protein with regard to its biological function or any disease or body condition that is associated with the isolated protein. Based solely on the fact that the protein was isolated from a cell membrane and it binds to protein X, applicant characterizes the isolated protein as receptor A. The function of protein X has also not been identified. The specification discloses a binding assay for determining other materials which bind to the receptor by adding the material to the complex of receptor A and protein X and determining the amount of inhibition of the binding of the complex as an indication that the material will bind to the receptor and thus be a therapeutic drug to effect control over the receptor. Also disclosed is the production of a monoclonal antibody that specifically binds to receptor A. There are no working examples using any materials to demonstrate such inhibition of binding, to assay the receptor or to identify any other material which binds to the receptor. The utility disclosed is for identifying materials that bind the receptor and the potential use of such materials as therapeutics.

#### **Claims:**

1. Isolated receptor A.
2. A method of identifying materials which bind to receptor A comprising:
  - a) forming a complex of receptor A and protein X in a liquid;

- b) adding a material to be screened to said complex;
- c) determining the amount of binding of said complex wherein an inhibition of said binding is an indication that said material binds to said receptor.

3. A monoclonal antibody which specifically binds to receptor A.

**Analysis:** The following analysis includes the questions that need to be asked according to the guidelines and the answers to those questions based on the above facts. For this fact situation, each claim will be analyzed separately.

**Claim 1:**

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to a property of the claimed receptor such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or provides any evidence that points to a property of the claimed receptor such that another non-asserted utility would be well established. Consequently, the answer to the question is no.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility for the claimed invention. In fact, for claim 1 there are two asserted utilities, i.e., a) a method of identifying materials which bind to receptor A, and b) a method of making a monoclonal antibody.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the method of identifying materials which bind to a specific receptor, namely receptor A and a method of making monoclonal antibodies to receptor A are methods that are not applicable to the general class of receptors. Therefore, there is an asserted specific utility for the claimed invention.

4) Is the asserted utility substantial? The answer to this question in each case is no. The method in 2a) above is a method of identifying those materials which bind to receptor A. Thus, to determine whether or not this method has a "substantial utility," it must be determined whether or not the material that binds to receptor A itself has a "specific and substantial utility." Here, the only utility asserted for the identified materials is a therapeutic to effect control over receptor A. Since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, a method of treating an unspecified, undisclosed disease or condition, does not define a "real world" context of use. Further research to identify or reasonably confirm a "real world" context of use is required. Since the asserted utility for the identified materials does not define a "real world" context of use, a method of identifying such materials also could not define a "real world" context of use.

The method in 2b) above is a method of making a material, i.e., a monoclonal antibody. Thus, to determine whether or not this method has a "substantial utility", it must be determined whether or not the monoclonal antibody itself has a "specific and substantial utility." Here, there is an asserted utility for the monoclonal antibody even though it is not explicit,

e.g., as a therapeutic drug to effect control over the receptor. However, since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case essentially is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition clearly would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that “Congress intended that no patent be granted on a chemical compound whose sole “utility” consists of its potential role as an object of use-testing”, and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Since the asserted utility for the product (monoclonal antibody) does not define a "real world" context of use, a method of making such a product also could not define a "real world" context of use.

Thus, the conclusion from analysis is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 1.

**Claim 2:**

1) Based on the record, is there a "well established utility" for the claimed invention? Since the claim is directed to a specific method of use, the utility of this claim is limited to that use and the examiner should not

look to a "well established utility" for the composition used in the claimed method. Consequently, there is no "well-established" utility for the method.

2) Has the applicant made any assertion of utility for the specifically claimed invention? Here, there is an asserted utility for the claimed invention, i.e., a method of identifying materials that bind to receptor A.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the method of identifying materials which bind to a specific receptor, namely receptor A, is a method that is not applicable to the general class of receptors. It is specific to receptor A. Therefore, there is an asserted specific utility for the claimed invention.

4) Is the asserted utility substantial? The answer to this question is no. Specifically, the method essentially is a method of identifying a material, i.e., those materials which bind to receptor A. Thus, to determine whether or not this method has a "substantial utility", it must be determined whether or not the material that binds to receptor A itself has a "substantial utility." Here, the only utility asserted for the identified materials is a therapeutic to effect control over receptor A. Since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case essentially is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition clearly would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole

“utility” consists of its potential role as an object of use-testing”, and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Since the asserted utility for the identified materials does not define a "real world" context of use, a method of identifying such materials also could not define a "real world" context of use.

Thus, the conclusion is that both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 2.

**Claim 3:**

1) Based on the record, is there a "well established utility" for the claimed invention? The specification as filed does not disclose or provide any evidence that points to a property of the claimed monoclonal antibody such that another non-asserted utility would be well established. Additionally, there is no art of record that discloses or provides any evidence that points to a property of the claimed monoclonal antibody such that another non-asserted utility would be well established. Consequently, the answer to the question is no.

2) Has applicant made any assertion of utility for the specifically claimed invention? Here, there is no explicitly asserted utility for the claimed monoclonal antibody. However, as stated in the analysis of claim 1 above, there is an implied asserted utility for the monoclonal antibody even though it is not explicit, e.g., as a therapeutic drug to effect control over the receptor.

3) Is the asserted utility specific? The answer to this question is yes. In this case, the monoclonal antibody is specific for a specific protein, namely receptor A. Therefore, there is an asserted specific utility for the claimed invention.

4) Is the asserted utility substantial? The answer to this question is no. Specifically, since neither the specification nor the art of record disclose any diseases or conditions associated with receptor A, the asserted utility in this case is a method of treating an unspecified, undisclosed disease or condition, which does not define a "real world" context of use. Treating an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. *See Brenner v. Manson*, 383 U.S. 519, 535–36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

Thus, both a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should be made on claim 3.

Caveat:

Let us assume for the moment that the specification also discloses that receptor A is present on the cell membranes of melanoma cells but not on the cell membranes of normal skin cells. Assume also that the examiner has found and made of record a journal article published prior to the